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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/703,399	10/31/2000	Li Zhu	25636-705	2855

21971 7590 06/17/2002

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EXAMINER

FRIEND, TOMAS H F

ART UNIT	PAPER NUMBER
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1627

DATE MAILED: 06/17/2002

6

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary*file copy*

Application No.

09/703,399

Applicant(s)

ZHU ET AL.

Examiner

Tomas Friend

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 March 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 54-61 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 54-61 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

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Detailed Action

Status of the Application

Receipt is acknowledged of a response to a restriction requirement on 28 march 2002 (Paper No. 5).

Status of the Claims

Claims 1-95 were pending in the present application. Claims 1-53 and 62-95 were cancelled as per applicants' request in Paper No. 5. Claims 54-61 are pending and examined on their merits.

Response to Restriction and Election of Species

Applicant's election without traverse of Invention III, claims 54-61 in Paper No. 5 is acknowledged.

Claims Rejections – 35 U.S.C. 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

1. Claims 54-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Motwani et al. U.S. Patent No. 6,358,733 B1 and Fusco et al. (1999) Yeast 15:715-720.

The Motwani et al. reference teaches the use of a yeast expression system for the expression of functional heterologous multi-domain proteins in yeast (abstract). Column 12, line 54 to column 14, line 46, teaches that chimeric antibodies are expressed from the same vector

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that contained two expression cassettes, each under the control of separate copies of the same promoter. The cloning of several different antibodies in which the heavy and light chains vary independently is taught in column 13, line 66 to column 14, line 8.

The Motwani et al. reference does not teach the use of linear insert and vector molecules, homologous recombination, or bicistronic expression.

The Fusco et al. reference teaches the in vivo construction of cDNA libraries for use in the yeast two-hybrid system (title). PCR is used to generate cDNAs that possess 5' and 3' flanking sequences that are homologous to the 5' and 3' sequences of a yeast expression vector. The flanking sequences range in length from 20 bp to 50 bp with 30 bp being the minimum length that maintains efficient recombination.

It would have been obvious to one of ordinary skill in the art at the time that the invention was made to use the cloning method of Fusco et al. to construct expression vectors analogous to those of Motwani et al. One would have been motivated to do so to replace the cumbersome cloning steps of Motwani et al. with a faster method that involved fewer method steps and could be used with any cDNA. One would have had a reasonable expectation for success because the cloning strategy of Fusco et al. and the expression system of Motwani et al. were both demonstrated to be functional. With respect to bicistronic expression, the choice of promoters as well as their placement would have been within the abilities of one of ordinary skill in the art to determine.

2. Claims 54-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Motwani et al. U.S. Patent No. 6,358,733 B1 and Kostrub et al. (1998) Nucleic Acids Research 26(20):4783-4784.

The Motwani et al. reference teaches the use of a yeast expression system for the expression of functional heterologous multi-domain proteins in yeast (abstract). Column 12, line 54 to column 14, line 46, teaches that chimeric antibodies are expressed from the same vector that contained two expression cassettes, each under the control of separate copies of the same promoter. The cloning of several different antibodies in which the heavy and light chains vary independently is taught in column 13, line 66 to column 14, line 8.

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The Motwani et al. reference does not teach the use of linear insert and vector molecules, homologous recombination, or bicistronic expression.

The Kostrub et al. reference teaches a method for making libraries of mutations in any specific gene for use in *S. pombe* (abstract). A gene of interest is amplified using PCR followed by cotransfection of the PCR products with a linear expression vector. The PCR products and linearized vector share homologous 5' and 3' flanking sequences of from 200-600 bp in length. Homologous recombination between the PCR products and linearized vector occur within the yeast cells.


It would have been obvious to one of ordinary skill in the art at the time that the invention was made to use the cloning method of Kostrub et al. to construct expression vectors analogous to those of Motwani et al. One would have been motivated to do so to generate mutated antibodies for screening, for example. The Kostrub et al. method would have replaced the numerous cloning steps of Motwani et al. with a faster method that involved fewer method steps and could be used to generate mutated libraries of any gene (including immunoglobulin heavy and light chains). One would have had a reasonable expectation for success because the cloning strategy of Kostrub et al. and the expression system of Motwani et al. were both demonstrated to be functional. With respect to bicistronic expression, the choice of promoters as well as their placement would have been within the abilities of one of ordinary skill in the art to determine.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Tomas Friend** at telephone number **(703) 308-4548**. The examiner can normally be reached on Monday, Tuesday, Friday, and Saturday 8:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist at (703) 308-1235.

Tomas Friend, Ph.D.
09 June 2002


DR. JYOTHSNA VENKAT-PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600